REMARKS

I. Status of Claims

Claims 21-32 and 34-40 are pending and are under consideration in the present application. Claims 21-32 and 34-40 stand rejected under 35 U.S.C. §101 as lacking credible, specific and substantial patentable utilities. Claims 21-32 and 34-40 stand rejected under 35 U.S.C. §112, first paragraph, as not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 21 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention.

Claim 21 has been amended to clarify that the polypeptide encoded by the claimed polynucleotide comprises residues 1-343 in one instance, 2-343 in another instance and 146-241 in a further instance. No new matter has been introduced by this amendment, which is being made solely for clarification. Support for this amendment is found throughout the specification as filed, for example on page 5, lines 19-22 and on page 4, lines 22-26, and in claim 21 itself.

II. Response to the Objections to the Specification

II.A. Sequence Rules

The U.S. Patent and Trademark Office ("the Patent Office") has objected to the Specification as being non-compliant with the rules governing sequences (37 C.F.R. §1.821-1.825) because nucleic acid and amino acid sequences presented in Figures 1, 2, 6 and 7 are not identified in the Figures with a SEQ ID NO identifier.

Applicants respectfully note, however, that these sequences are reported with their respective SEQ ID NO identifiers in the "Brief Description of the Drawings" section of the specification. Further, each sequence that appears in the objected-to Figures is included in the Sequence Listing filed with the present patent application. Applicants therefore submit that since the sequences appearing in the objected-to Figures are identified by SEQ ID NO in the body of the Specification and in the Sequence Listing, the Specification is in compliance with the requirements of 37 C.F.R. §1.821-1.825. Applicants respectfully request that this objection be withdrawn.

II.B. URL's

The Patent Office has objected to the Specification because it contains browser-executable code, per MPEP 608.01(p).

Applicants have amended the Specification to remove all references to browser-executable code.

III. Response to the Rejection of Claims 21-32 and 34-40 Under 35 U.S.C. §101

It is the Patent Office's position that "the specification does not disclose the function of the ion-channel-like polypeptide in the context of the cell or organism." Official Action, page 4. The Patent Office also states, " very little information is known about the channel except the sequence data and no function has been attributed to it." Official Action, page 4. The Patent Office continues, "[s]ignificant further experimentation would be required of the skilled artisan to identify any function associated with the ion-channel-like polypeptide or the polynucleotide encoding it." Official Action, page 4.

The Patent Office then discusses each of several identified utilities. Summarily, it is the Patent Office's position that the use of the claimed polynucleotides and/or polypeptides in (1) the

treatment of potassium ion-channel polypeptide deficiency is not substantial; (2) the use of the molecules in the production of antibodies is not specific; (3) the use of the molecules to produce a variant nucleotide and polypeptide is not substantial or specific; (4) the use of the molecules to search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide is not substantial; and (5) the use of the molecules in tissue typing is not substantial or specific. Applicants respectfully traverse the rejection and submit the following comments.

Initially, attention is directed to the Revised Interim Utility Examination Guidelines ("the Utility Guidelines"). It is well established that when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the Examiner unless the Patent Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." Fujikawa v Wattanasin, 93 F.3d 1559, 1565, 39 U.S.P.Q.2d 1895, 1900 (Fed. Cir. 1996).

Bearing the above comments and precedent in mind, the Patent Office's rejections under 35 U.S.C. §101 will be addressed individually in the following paragraphs.

(1) The Patent Office states,

> The specification does not disclose any conditions wherein there is a deficiency of the claimed polynucleotides or polypeptides. Significant further experimentation would be required of the skilled artisan to identify individuals who would benefit from such a compound and then to determine a best course of treatment. There is no disclosure, for example, of dosages, how to assay for improvement or intolerable side effects, etc.

Official Action, page 5. The Patent Office then concludes the asserted utility is not substantial.

Applicants respectfully disagree. Applicants direct attention to page 48, lines 30-34 of the specification, wherein Applicants state "[b]ased on the expression pattern of this novel sequence, diseases that can be treated with agonists and/or antagonists for K+betaM5 including, but not limited to, epilepsy, Bartter's syndrome, persistent hyperinsulinemic hypoglycemia of infancy, hyperkalemia and hypokalemia, cystic fibrosis and hypercalciuric nephrolithiasis." Applicants also direct attention to page 49, line 36 to page 50, line 9 of the specification, wherein

Applicants state "antagonists of K+betaM5 may be useful in the treatment of inflammatory diseases including rheumatoid arthritis, asthma, multiple sclerosis, osteoarthritis, among others. Thus, agonists of K+betaM5 may enhance an individual's immunity after vaccination. In contrast, antagonists of this K+betaM5 could be useful for treating T-cell mediated autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, psoriasis, among others."

Thus, contrary to the Patent Office's assertion, the specification does, in fact, disclose conditions in which an ion channel deficiency, such as a condition associated with a deficiency in a polypeptide or polynucleotide of the present invention, might be treated using a modulator produced in accordance with the present invention.

Applicants also assert that the recited utility is substantial. According to the Utility Guidelines, an assay method for identifying compounds that themselves have a substantial utility defines a "real world" context of use. Utility Guidelines, page 6. Applicants assert that the compounds identified by the claimed method meet the substantial utility test because they are useful for treating specific disorders, such as epilepsy, Bartter's syndrome, persistent hyperinsulinemic hypoglycemia of infancy, hyperkalemia and hypokalemia, cystic fibrosis and hypercalciuric nephrolithiasis.

Applicants also disagree with the Patent Office's conclusion that significant experimentation would be required to identify individuals who would benefit from a compound produced in accordance with the present invention and to determine a best course of treatment. Applicants submit that any such experimentation, if in fact any is required, would be simply routine and is unnecessary to identify or confirm a "real world" context. Applicants submit that a "real world" context is already established and no further experimentation is required in this regard.

(2) With respect to the recited utility of producing antibodies, the Patent Office states:

> This asserted utility is credible and substantial but not specific. Antibodies can be made to any polypeptide. However if the specification discloses nothing specific and substantial about the polypeptide, but the polypeptide and the antibodies have no patentable utility.

Official Action, page 5.

Applicants respectfully disagree with the Patent Office's conclusion. Applicants submit that specific and substantial details regarding the claimed polynucleotides and polypeptides is

provided in the specification as filed. For example, tissue profiling was performed that localized expression of the claimed polypeptides to testis, spinal cord, lymph node, heart, uterus, and to a lesser extent, in small intestine, stomach, prostate, and kidney (see Figure 8). Expanded expression profiling (see Figure 9) confirmed high expression in testis. Further, RNAi data on protein CG10465, the putative *Drosophila* ortholog of the claimed human K+betaM5, indicates that in *Drosophila* this protein regulates the LPS-response pathway (see page 49, lines 16-26).

This data provides specific and substantial details regarding the claimed polypeptides and polynucleotides of the present invention. Thus, contrary to the Patent Office's position, the specification does indeed provide specific and substantial details of the claimed polynucleotides and polypeptides of the present invention. Consequently, Applicants submit that the antibodies of the present invention, as well as the polypeptides, have utility that is specific, substantial and credible.

(3) Next, the Patent Office argues the asserted utility of producing a variant nucleotide and/or polypeptide is credible but not substantial or specific. It is the Patent Office's position that

> [T]he specification discloses nothing specific or substantial for the variant nucleotide and polypeptide that is produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

Official Action, page 5-6. Applicants strongly disagree with the Patent Office's conclusion.

The Patent Office contends the asserted utility is not present in a mature form that can be used in a "real world" sense. Applicants strongly disagree with the Patent Office's position. As noted above, the polypeptides and polynucleotides of the present invention have been specifically and substantially described in the specification. This knowledge can be employed to make, study and use variants of the claimed polypeptides and polynucleotides. Indeed guidance is provided in the specification (see page 89, line 18 through page 90, line 12, including Table 3 presented therein, for example) in preparing such variants. Such variants can be employed in the same roles as the characterized claimed polypeptides and polynucleotides. For instance, a variant prepared in accordance with the present invention might exhibit an enhanced activity that might be desirable in a given application of the sequences of the present invention.

Apparently, it is the Patent Office's position that since no variant of the claimed polypeptide was actually produced and characterized, the polypeptide of the present invention has no utility. Applicants respectfully remind the Patent Office that there is no requirement that an applicant provide any working examples. This rule is applicable regardless of the context in which it is applied. Thus, Applicants submit that a rejection based on the Patent Office's argument that a variant of the claimed polypeptide having an arbitrary utility was not produced and characterized cannot stand.

(4) The Patent Office then argues the recited utility of screening for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide is credible and specific but not substantial. The Patent Office contends

> The specification does not characterize the polypeptide encoded by the polynucleotide of the claimed invention. Therefore binding sites, etc. are not identified. Significant further experimentation would be required of the skilled artisan to characterize the protein and search for ligands. There is no disclosure for example, of how to assay for ligand binding and possible transduction mechanisms. It is not know the class of drugs to use or what measurements to perform.

Official Action, page 6. Again, Applicants strongly disagree with the Patent Office's position.

As described above, Applicants have characterized the claimed polypeptides and polynucleotides, particularly in terms of localized expression. Applicants have also provided RNAi data related to the putative *Drosophila* ortholog of the claimed polypeptides.

Applicants submit that knowledge of the precise nature of the binding site(s) of the claimed invention is not required to practice screening methods involving the claimed polypeptide. It is not necessary to precisely characterize a binding site and to identify which residues are involved in a binding reaction in order to detect a binding event and/or to perform a screening operation. With respect to the Patent Office's contention that the specification provides no disclosure on how to assay for ligand binding, Applicants direct attention to the section beginning on page 210, line 21 entitled "Binding Assays." In this section Applicants provide direction on how to set up and perform various ligand binding assays designed to identify modulators of K+betaM5 activity.

Applicants therefore submit that the asserted utility is in fact substantial, credible and specific.

(5) Lastly, the Patent Office contends the recited utility of tissue typing is credible but not substantial or specific. The Patent Office argues

> [P]atentable utility of tissue typing for the polynucleotide encoding the claimed polypeptide is not substantial because one skilled in the art would not readily use the nucleotide sequences for tissue typing in a real world sense as the protein is not specific to one tissue and is not associated with any disease or disorder. This asserted utility is also not specific because numerous unrelated nucleotide sequences would also show a similar tissue typing pattern.

Official Action, page 6-7. Applicants do not agree with the Patent Office's conclusion.

Applicants submit that tissue typing is a "real world" context of use and is supported by the present specification. First, as Applicants have noted above, data provided in the specification indicates the claimed polypeptide is expressed in lymph node tissue. Next, RNAi studies indicate that the putative *Drosophila* ortholog regulates the LPS-response pathway. Further, the RNAi data (see Example 6) support the proposition that the claimed human ortholog of the *Drosophila* CG10465 polypeptide, namely K+betaM5, is involved in the NF-κB pathway. The NF-κB pathway is associated with a variety of disorders, including immune disorders. Applicants recite several immune system conditions, for example, rheumatoid arthritis, asthma, multiple sclerosis, osteoarthritis, in which the claimed polypeptide might be implicated. These immune system conditions are significant and substantial.

With regard to all utilities recited in the specification, Applicants also respectfully remind the Patent Office that it has the burden of demonstrating that the assertions of made by an applicant might be doubted by one of ordinary skill in the art. As stated by the C.A.F.C., "the PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. . . Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

Thus, the Patent Office must treat as true a statement of fact made by Applicants in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. Further, the *Brana* court indicated that unless the invention involves an inherently

unbelievable undertaking or involves implausible scientific principles, or is contravened by evidence proffered by the Patent Office, an asserted utility must be accepted. *Id.*

In the present case, Applicants respectfully submit that the Patent Office has provided only speculation, and no such countervailing evidence has been provided. If such evidence is available to the Patent Office, Applicants request that the Patent Office provide an affidavit pursuant to 37 C.F.R. § 1.104(d)(2) containing evidence substantiating this position.

Summarily, in view of the above, Applicants submit that each of the utilities provided in the specification, including those identified by the Patent Office, are specific, substantial and credible. Accordingly, applicants respectfully request that the rejection of claims 21-32 and 34-40 under 35 U.S.C. §101 be reconsidered and withdrawn. Applicants further submit that claims 21-32 and 34-40 are in condition for allowance and courteously solicit the same.

III. Response to the Rejection of Claims 21-32 and 34-40 Under 35 U.S.C. §112, First Paragraph

The Patent Office rejected claims 21-32 and 34-40 under 35 U.S.C. §112, first paragraph for various enumerated reasons. Applicants respectfully traverse the rejection and submit the following comments, which, for clarity, are directed to the rejections in the order the Patent Office presented them. Before addressing the specific rejections, Applicants submit the following general comments.

Initially, Applicants note that, with respect to the written description requirement of 35 U.S.C. §112, first paragraph, it is the Patent Office's burden to establish a *prima facie* case of unpatentability with respect to Applicants' presumptively adequate written description ("As in cases involving the enablement requirement of § 112 . . . we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." *In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976).). Applicants submit that in the present case, particularly in view of the remarks made herein above regarding several recited utilities, the Patent Office has not demonstrated that one of ordinary skill in the art would not conclude that Applicants have possession of the claimed invention described in the specification as filed and therefore that the Patent Office has not met this burden.

Further, Applicants note that courts have repeatedly held that the question of whether the written description requirement is met depends on what a person of ordinary skill in the art would understand, based on consideration of the specification, and not on the explicit disclosure of particular embodiments. See, e.g., *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000); *In re Hayes Microcomputer Prods., Inc.*, 982 F.2d 1527, 25 U.S.P.Q.2d 1241 (Fed. Cir. 1992).

With regard to the enablement requirement, Applicants submit that, as a matter of Patent Office practice, the burden rests upon the Patent Office to establish a *prima facie* case of a failure to comply with 35 U.S.C. § 112, first paragraph, with respect to the invention described and claimed in applicants' presumptively enabling patent application. *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1971), *In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976). More specifically, the Patent Office bears the burden of establishing by a preponderance of evidence that one of ordinary skill in the art would not be enabled to practice the present invention after considering the present disclosure in combination with what is known in the art.

Continuing, with regard to the enablement requirement, Applicants respectfully submit that in its formulation of the rejection of claims 21-32 and 34-41 under 35 U.S.C. §112, first paragraph, the Patent Office has adopted an inappropriate standard for measuring enablement. More particularly, it appears that the Patent Office has not given due weight what is known in the art. The appropriate standard is that the claimed invention must be enabled so that a person skilled in the art can make and use the invention from the disclosures of the present U.S. patent application, coupled with information known in the art, without "undue experimentation." *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988).

It is Applicants' position that the Patent Office has failed to give due weight to what is known to those of ordinary skill in the art when it formulated its rejections under 35 U.S.C. §112, first paragraph. Applicants again note that the Patent Office's burden is to demonstrate that the disclosure combined with what is known in the art does not enable one of ordinary skill in the art to practice the invention commensurate with the scope of the claims. Applicants submit that although the Patent Office has presented a general discussion of pertinent factors involved in making an enablement analysis, the Patent Office has not provided any concrete evidence that one of ordinary skill in the art would not be enabled by the present disclosure,

combined with what is known in the art, to employ the compositions and methods of the present disclosure, particularly in view of the specific, substantial and credible utilities recited in the specification.

Applicants now respond to the specific rejections made by the Patent Office.

(1) First the Patent Office rejected claims 21-32 and 34-40 under 35 U.S.C. §112, first paragraph as "not supported by either a specific and substantial asserted utility or a well established utility." Official Action, page 7.

For the reasons discussed above, Applicants submit that the present invention is supported by a specific and substantial utility, and also satisfies the requirements of 35 U.S.C. §112. Applicants submit that the specification of the present application teaches the manner in which to make and use the present invention. The present application describes how to make or obtain the claimed nucleic acids, vectors and host cells. In addition, the present application discloses how to use the isolated nucleic acids encoding K+betaM5 and variants thereof, recombinant vectors and host cells containing the nucleic acid to make K+betaM5 polypeptides, and to identify modulators thereof useful for the treatment of various disorders, notably immune system disorders.

(2) The Patent Office's next rejection of claims 21-32 and 34-40 under 35 U.S.C. §112, first paragraph, it is the Patent Office's position that "the specification does not teach functional or structural characteristics of the claimed polynucleotide" and that "function cannot be predicted based solely on structural similarity to a protein found in the sequence databases." Official Action, page 7.

In this regard, it appears that the Patent Office is requiring that Applicants submit working examples in order to comply with the requirements of 35 U.S.C. §112, first paragraph. However, no such requirement is recited by the applicable statute or case law. While the presence or absence of working examples can be a consideration in the overall evaluation of enablement, working examples are not required under 35 U.S.C. §112, first paragraph, to comply with the enablement standard presented therein. Indeed, the M.P.E.P. states that a U.S. patent application need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *M.P.E.P. §2164.02.*

To support its position, the Patent Office has presented several references in which it is stated that knowing a polypeptide's structure is insufficient to fully characterize the polypeptide. However, Applicants remind the Patent Office that the literature is replete with examples in which function was predicted on the basis of structural similarity, and was later confirmed experimentally.

Applicants further submit that a detailed characterization sufficient to practice the invention as claimed has been provided. In the present application, for example, the claims are directed to isolated K+beta M5 polypeptides and polynucleotides encoding these proteins, as well as to host cells and vectors. In order to practice these claims, a detailed knowledge of the precise mechanism by which ions are transported is not required.

(3) The Patent Office then contends Applicants' assertion that the claimed polynucleotide encodes an ion channel "cannot be accepted as credible in the absence of supporting evidence of specific function because the art shows that structurally similar ion channels are unpredictably functionally dissimilar." Official Action, page 8.

As Applicants have argued throughout the present Response, the Patent Office has not offered any concrete evidence that calls into doubt Applicants asserted function for the claimed polynucleotides and polypeptides. To the contrary, the references the Patent Office cites to support this conclusion offer mere speculation and do not specifically address the situation in which a protein is predicted by its sequence to comprise a potassium channel, but in actuality has another function.

For example, the Lehmann-Horn et al. reference cited by the Patent Office (Lehmann-Horn et al., (1999) *Physiol. Rev.* 79(4):1317-1372) discusses the sub-classification of potassium channels, but does address the question of whether a given sequence does or does not comprise a potassium channel. Thus, although the group of potassium channels might be a diverse group, this does not call into question their role as potassium channels. Further, even if the Patent Office is correct in its statement that the identified channels are involved in a variety of cellular functions, this does not necessarily mean they cannot be functionally characterized as ion channels.

Applicants reiterate that Applicants' assertion that the claimed polynucleotide encodes an ion channel has not been seriously called into question by the references supplied by, or the

arguments presented by, the Patent Office. Absent any concrete and substantial evidence to the contrary, Applicants respectfully remind the Patent Office that it is obligated to accept Applicants' assertions as true and thus credible.

(4) The Patent Office then reiterates its arguments regarding the utility of the claimed polynucleotides and polypeptides and concludes "membership in a class of ion channels may not impart a specific, substantial and credible utility to a new member, such as the claimed polynucleotide of the instant Application." Official Action, page 9.

Applicants reiterate the arguments presented above regarding the utilities presented in the specification, including those enumerated by the Patent Office. Summarily, Applicants submit that the characterization of a sequence as an ion channel is, in and of itself, a specific, substantial and credible utility, particularly in the case in which the ion channel is identified (by whatever means) as a particular type of ion channel. Moreover, the identified channels can be employed in the recited uses. But the present invention goes further and asserts not only that the claimed sequence is an ion channel but that it is a particular type of ion channel, namely a potassium channel.

Moreover, the utility of the present invention is not tied exclusively to membership in a class of ion channels. Indeed, the sequences of the present invention can be employed in a range of applications that can, but are not required to, depend on the identification of the claimed polypeptide as an ion channel. For example, the production of antibodies to the claimed sequence does not absolutely require that the sequence is an ion channel, since such antibodies can be employed in applications that are independent from the identity of the sequence.

(5) Next, the Patent Office states that it would require "undue experimentation to determine with the specific biological activities of the polypeptide are." Official Action, page 9.

The Utility Guidelines require that Applicants need only provide one credible assertion of specific and substantial utility to satisfy the utility requirement. The Patent Office's position appears to be that the biological functionality of K+betaM5 must be completely characterized and demonstrated in one or more examples before utility is established. However this requirement is not the law and Applicants further submit that it is also not the current standard

set forth by the Patent Office. For the reasons discussed above, Applicants submit that the claimed invention is, in fact, supported by at least one specific, substantial and credible utility.

Turning next to the Patent Office's assessment of the level of experimentation required to practice the claimed invention ("[T]he specification fails to teach the skilled artisan how to use the claimed polynucleotides to make a biologically active ion channel-like polypeptide without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are." Official Action, page 9), it is Applicants' position that, even if it might require experimentation to use the claimed polynucleotides, the quantity of experimentation to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni*, 195 U.S.P.Q. 150, 153 (C.C.P.A. 1977). "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the U.S. patent application in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed." *In re Wands*, 8 U.S.P.Q.2d at 1404 (citing *In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976)).

The specification provides a nucleic acid sequence encoding the claimed K+betaM5 polypeptide, as well as the sequence of the claimed polypeptide itself. Contrary to the Patent Office's position, no experimentation is required, beyond the application of routine molecular biological techniques, in order to use the claimed polynucleotides to make a biologically active ion channel-like polypeptide. If additional experiments are pursued to identify additional biological activities of the expressed polypeptide, the guidance provided by the specification would provide the skilled artisan with all necessary guidance to characterized any such activity. For example, the specification discloses the homology between the claimed polynucleotides and polypeptides with a variety of ion channels (see page 47, line 34 to page 48, line 15). Using the guidance of the specification, for example the disclosed homology, coupled with established techniques for the study of ion channels, such as patch-clamp methodology, one of ordinary skill in the art could readily practice the claimed invention.

(6) The Patent Office again asserts "[t]he specification does not teach the skilled artisan how to use the claimed polynucleotides encoding the ion channel-like polypeptide for any purpose." Official Action, page 9.

Applicants again reiterate that the specification does indeed teach the skilled artisan how to use the claimed polynucleotide, in fact for a range of uses. For example, as argued herein above, the specification provides adequate guidance to those of ordinary skill in the art to make and use the claimed sequences (a) to produce molecules useful for the treatment of potassium ion-channel polypeptide deficiency, of which the specification identifies several, (b) for the production of antibodies, (c) to produce a variant nucleotide and polypeptide, (d) to search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide and (e) in tissue typing, among other uses. These are all specific, substantial and credible uses of the claimed sequences.

(7) The Patent Office also contends "the instant application does not reasonably provide enablement for various nucleotide forms of SEQ ID NO:23, wherein the sequence is at least 60% identical to the nucleotide of SEQ ID NO:23" Official Action, Page 10. The Patent Office concludes "[t]here are no examples of what specific polynucleotides fall within the range of those that would be 60% identical. Neither is it clear if this percent identify need be over a contiguous region or a specific portion of the protein." Official Action, page 11.

Additionally, for the reasons discussed above, Applicants submit that there is no requirement that Applicants provide specific examples of specific polynucleotides that fall within the range of those that would be 60% identical.

With respect to the Patent Office's question as to whether the percent identity need be over a contiguous region or a specific portion of the protein, Applicants direct attention to page 83, line 33 through page 84, line 12 of the specification. Herein Applicants recite that a percent identity can " occur at the amino- or carboxy-terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence."

Additionally, Applicants provide a specific method of calculating identity, namely by employing a CLUSTALW global sequence alignment. More particularly, in addition to

describing methods of determining identity in the specification, claim 37 specifically recites the use of a CLUSTALW global sequence alignment. A detailed description of the nature and use of the CLUSTALW alignment, including an example, is provided in the specification on pages 82, line 33 through page 83, line 32. Thus, one of ordinary skill in the art is provided with yet more guidance with which to practice the claimed invention.

(8) The Patent Office then argues, with respect to claims 37-40, that "the claimed invention is not supported by either a specific asserted utility or a well established utility." Official Action, page 11.

Applicants again reiterate the above arguments that the claimed invention is indeed supported by specific, substantial and credible utility, for example those identified by the Patent Office, namely (a) to produce molecules useful for the treatment of potassium ion-channel polypeptide deficiency, of which the specification identifies several, (b) for the production of antibodies, (c) to produce a variant nucleotide and polypeptide, (d) to search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide and (e) in tissue typing, among other uses. As argued above, Applicants submit that these and other utilities are supported by the specification as filed.

(9) The Patent Office has also rejected claims 37-40 "as containing subject matter which was not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention." Official Action, page 12. It is the Patent Office's position that "the specification does not teach functional or structural characteristics of the claimed polynucleotides. The description of one polynucleotide encoding a potassium channel polypeptide (SEQ ID NO:23) is not adequate written description of an entire genus of functionally equivalent polynucleotides. and polypeptides." Official Action, page 13

Applicants note that the *Guidelines for Examination of Patent Applications Under the 35 USC 112, ¶1 "Written Description" Requirement* indicate that the written description requirement can be satisfied by "sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure of relevant, identifying characteristics." *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1*

"Written Description" Requirement, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001). See also, *University of California v. Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) and *MPEP* §2163.II.A.ii.

Applicants submit that the specification as filed discloses an extensive list of representative species and relevant characteristics of the species, thereby satisfying the written description requirement of 35 U.S.C. §112, first paragraph. Particularly, Applicants direct attention to pages 63-66 of the specification, wherein an extensive list of N-terminal and C-terminal deletion polypeptides are disclosed. The specification states "polynucleotide sequences encoding these polypeptides are also provided" (Specification, page 66, line 22). These deletion polypeptides comprise fragments of the nucleic acid and polypeptide sequences of SEQ ID NOs:23 and 24. These polynucleotide sequences (a) would be expected to hybridize under stringent conditions (which are described in the specification, for example on page 18, line 33 and ending on page 19, line 5, and on page 74, line 8 and ending on page 77, line 12, including Table 2 presented therein) to the polynucleotides specified in (a)-(f) of claim 21 (recited in claim 37), (b) have a nucleotide sequence that is at least 60% identical to a sequence provided in claim 21 (recited in claim 37); and (c) do not encode the polypeptide set forth as SEQ ID NO:24. Therefore, the amino acid and/or polynucleotide sequences are representative of the claimed genus.

Applicants further note that in addition to the disclosed N- and C-terminal deletion polynucleotides, the specification describes the use of conservative substitutions in generating variants of the polynucleotides and polypeptides of the present invention (page 89, line 18 through page 90, line 12, including Table 3 presented therein). Such variants can have a different sequence from that of SEQ ID NO:24, yet retain the properties recited in claim 21, and thus claims 37-40 which depend directly or indirectly therefrom. Thus, this group of variants highlights yet more species that are representative of the claimed genus.

Next, Applicants draw attention to the statement that "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosures necessary to satisfy the written description requirement." *Guidelines for Examination of Patent Applications Under the 35 USC 112, ¶1 "Written Description" Requirement*, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001). As noted, Applicants submit that the relative level of skill in the pertinent field is very high. Therefore, Applicants submit that given the high level of skill in the field

identified by the Patent Office, the large number of species representative of the claimed genus disclosed in the present specification, coupled with the discussion of their relevant identifying characteristics, the invention is fully described in accordance with 35 U.S.C. §112, first paragraph.

Applicants submit that, in view of (a) the extensive disclosure of N- and C-terminal deletion polypeptides and the polynucleotides that encode these polypeptides, presented in the specification, (b) the disclosure of species comprising conservative substitutions of SEQ ID NO:24, (c) the recitation of identifying characteristics of the members of the claimed genus, and (d) the high level of skill in the art, claims 37-40 are in accord with the Written Description Guidelines and the pertinent case law (see, e.g., *University of California v. Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997)), and that the written description requirement of 35 U.S.C. §112, first paragraph, has been met. Summarily, Applicants submit that one of ordinary skill in the art would recognize that Applicants had invented what was claimed, which is the standard against which the adequacy of a written description is gauged. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). Accordingly, Applicants respectfully request that the rejection of claims 37-40 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn. Applicants further submit that claims 37-40 are in condition for allowance and respectfully solicit the same.

Accordingly, for the reasons presented above, Applicants respectfully request that the rejection of claims 21-32 and 34-40 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn. Applicants further submit that claims 21-32 and 34-40 are in condition for allowance and respectfully solicit the same.

IV. Response to the Rejection of Claim 21 Under 35 USC 112, Second Paragraph

Claim 21 has been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter that applicant regards as the invention.

More particularly, the Patent Office has rejected "claim 1" for reciting the terms "complimentary" and "antisense" in the same claim. It is the Patent Office's position that the term "antisense" is a narrower statement that the term "complementary" and has accordingly rejected the claim as indefinite. Applicants first submit that Claim 1 was cancelled by the

previously filed Preliminary Amendment. For purposes of being fully responsive to the present Official Action, Applicants assume that the Patent Office intended that this rejection be directed to claim 21, which was added in the Preliminary Amendment.

Although Applicants disagree with the Patent Office's characterization of the scope of the terms "complementary" and "antisense," claim 21 has been amended to remove the recitation of the term "antisense."

Next the Patent office rejected claim 21 as indefinite for reciting the term "corresponding to" in the recitation "a polypeptide corresponding to amino acids 146 to 241." Applicants submit that the meaning of the term is clear and those of ordinary skill in the art, upon consideration of the specification, would recognize that the term refers to a polypeptide comprising amino acids 146-241. As described in the specification, the present invention encompasses sequences that are identical to, as well as sequences that are similar to, the recited sequence. Applicants have, however, amended claim 21 to replace the term "corresponding to" with the term "comprising" solely to clarify the identity of the peptide encoded by the claimed nucleic acid.

Lastly, the Patent Office asserts claim 21 is indefinite for reciting the term "stringent conditions," which the Patent Office argues is a conditional term. Applicants respectfully direct attention to the discussion beginning on page 18, line 33 and ending on page 19, line 5, wherein Applicants define "stringent hybridization conditions." Further discussion and definition of "stringent conditions" is provided in the section beginning on page 74, line 8 and ending on page 77, line 12, including Table 2 presented therein.

Applicants submit that in view of the amendments to claim 21 and the remarks presented above, claim 21 is in full compliance with 35 U.S.C. §112, second paragraph. In view of the amendments and remarks presented herein, Applicants respectfully request that the rejection of claim 21 under 35 U.S.C. §112, second paragraph be withdrawn. Applicants further submit claim 21 is in condition for allowance and courteously solicit the same.

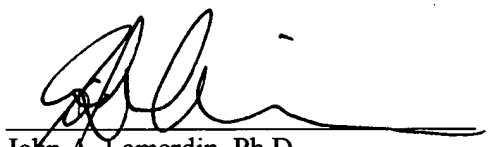
V. Conclusions

In light of the above amendments and remarks, Applicants respectfully request that the rejections of record be withdrawn. Applicants further submit that the subject patent application is in condition for allowance and courteously solicit a Notice of Allowance.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

Although it is believed no additional fee is due, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment associated with the filing of this correspondence to Deposit Account Number 19-3880 in the name of the Bristol-Myers Squibb Company.

Respectfully submitted,



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